



NOTES HERPESVIRUSES

MICROBE OVERVIEW

- Large family of DNA viruses

Species known to infect humans

- Herpes simplex virus (HSV)
 - HSV-1, HSV-2
- Varicella-zoster virus (VZV)
- Epstein-Barr virus (EBV)
- Human cytomegalovirus
- Human herpesvirus 6 (roseola)
- Human herpesvirus 8 (Kaposi's sarcoma)

Genetic material

- Double-stranded, linear DNA genome encoding 84 proteins

Morphology

- Icosahedral capsid; enveloped virus

Life cycle

- Obligate intracellular parasites
- Can perpetuate in latent phase
- Expression of lytic genes → lytic phase → host cell death → shedding

CYTOMEGALOVIRUS

osms.it/cytomegalovirus

PATHOLOGY & CAUSES

- Primary infection of immunocompetent individuals usually asymptomatic; lifelong latency
- Infects mononuclear leukocytes, endothelial cells

CAUSES

- Person-to-person transmission
 - Kissing; intimate, sexual contact
- Vertical transmission
 - Congenital infection
- Blood products/transfusion
- Organ/stem cell transplant

RISK FACTORS

- Immunocompromised
 - HIV/AIDS; organ transplant; medications (e.g. steroids, chemotherapy)

COMPLICATIONS

- Congenital CMV infection
 - Cognitive, sensorineural deficits

SIGNS & SYMPTOMS

- Usually asymptomatic
- Fever, malaise, sore throat, splenomegaly
- Individuals with AIDS
 - Retinitis, colitis, encephalitis, pneumonitis
- Individuals with congenital CMV infection
 - Positive CMV-IgG (if pregnant); intrauterine fetal growth restriction (IUGR), hydrocephalus, microcephaly, intracranial calcification, poly/oligohydramnios, hepatosplenomegaly

VISIT...

LANZAROTE
Caliente.COM

DIAGNOSIS

LAB RESULTS

- Complete blood count
 - Atypical lymphocytosis, anemia, leukopenia, thrombocytopenia
- ↑ serum creatinine, AST, ALT
- Serology tests
 - ↑ CMV-IgM titre; acute infection
 - ↑ CMV-IgG titre; past infection

TREATMENT

- Usually self-limiting

MEDICATIONS

- At-risk individuals
 - Antiviral prophylaxis; IV ganciclovir; oral valganciclovir

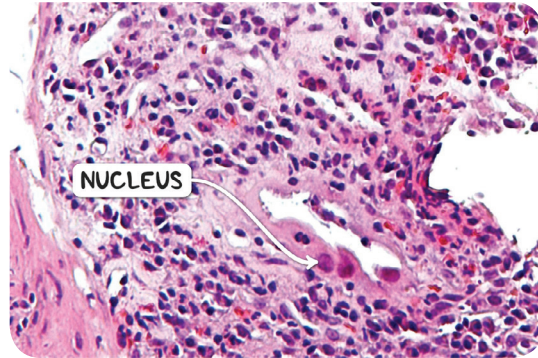


Figure 79.1 A colonic biopsy taken from an individual with CMV colitis. The large nuclei that give the virus its name can be clearly seen.

EPSTEIN–BARR VIRUS (INFECTIOUS MONONUCLEOSIS)

osms.it/epstein-barr_virus

PATHOLOGY & CAUSES

- EBV (human herpesvirus 4)
- Causes Infectious mononucleosis (glandular fever)
- Infection in children
 - Asymptomatic/mild flu-like symptoms
- Infection in adolescents, young adults
 - Fever, sore throat, enlarged lymph nodes
- Lytic, latent life cycle
 - Lytic in oropharyngeal B cells; latent in lymphocytes

CAUSES

- Transmitted through saliva (“kissing” disease), sexual transmission

RISK FACTORS

- Multiple sexual partners

COMPLICATIONS

- Splenic rupture
- EBV infection associated with Hodgkin’s, Burkitt’s lymphoma
- Neurologic syndromes (2–4 weeks after initial symptoms)
 - Guillain-Barré syndrome, cranial nerve palsies (e.g. facial nerve palsy); meningoencephalitis (e.g. aseptic meningitis), transverse myelitis, peripheral neuritis, optic neuritis
- EBV can affect, manifest in any organ system
 - Hepatitis, pneumonia, myocarditis, pancreatitis, acute renal failure, gastric pseudolymphoma

SIGNS & SYMPTOMS

- Classic triad
 - Fever; cervical/generalized lymphadenopathy; tonsillar pharyngitis (exudative/non-exudative)
- Malaise, hepatosplenomegaly, rash, jaundice, myalgia

- morphology (large, irregular nuclei)
- ↑ hepatic transaminase (50% of infected individuals)
- Monospot test
 - Positive heterophile antibodies (IgM)
- Identification of EBV
 - EBV-specific antibodies, real-time PCR, EBV DNA detection

DIAGNOSIS

LAB RESULTS

- Complete blood count (CBC)
 - Lymphocytosis (50%) with atypical

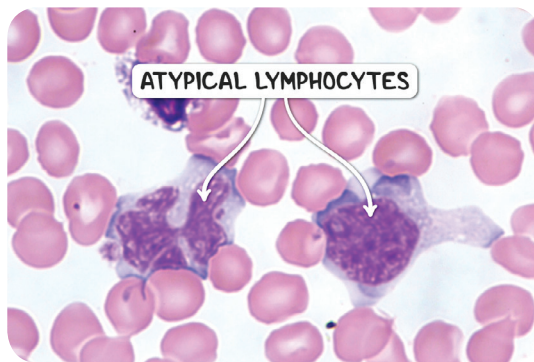


Figure 79.2 Atypical lymphocytes with bizarre nuclear forms in a peripheral blood film from an individual infected with infectious mononucleosis.

TREATMENT

MEDICATIONS

- Antipyretics, analgesics
 - Avoid aspirin; may lead to Reye's syndrome
- Corticosteroid for upper airway obstruction (e.g. prednisolone)
- Intravenous immunoglobulin (IVIG) for thrombocytopenia

HERPES SIMPLEX VIRUS

osms.it/herpes-simplex-virus

PATHOLOGY & CAUSES

- HSV-1, HSV-2
 - Members of herpesviridae family
- Causes oral, genital, ocular ulcers
- Portal of entry
 - Mucosal surfaces/skin breaks; vertical transmission during pregnancy/childbirth

- Primary infection often symptomatic; replicates in epidermis of skin → travels down nerve endings, axon → sensory ganglia
- Periodic reactivation, subsequent episodes
 - Virus becomes active in ganglia → transported via axon to skin → replicates in epidermis → sheds → new sores
 - Often asymptomatic shedding; may feel tingling, burning sensation

TYPES

- Infection types
 - **Primary:** first infections; seronegative; symptoms more extensive, systemic; greater viral shedding loads
 - **Non-primary:** previously infected individuals; serum antibody, humoral immunity (e.g. genital HSV-2 infection in adulthood after oral mucosa HSV-1 infection in childhood)
 - **Recurrent:** previously infected individuals; reactivation episodes (e.g. genital HSV-2 infection in adulthood after genital HSV-2 infection in adolescence)
- **Herpes labialis** (AKA oral herpes)
 - HSV-1 infection of oral mucosa, lips
- **Genital herpes**
 - HSV-2, HSV-1 infection of genital area
 - Healing takes 2–4 weeks

CAUSES

- Portal of entry
 - Mucosal surfaces/skin breaks; vertical transmission during pregnancy/childbirth
- Spread person to person; **sexual transmission**

RISK FACTORS

- Genital herpes
 - Contact with infected individual (producing, shedding virus)
 - Immunosuppression (e.g. medications, HIV/AIDS)
 - High-risk sexual behavior (e.g. multiple sexual partners, unprotected intercourse, first sexual activity at early age)

COMPLICATIONS

- Neonatal HSV infection, meningitis, encephalitis, acute retinal necrosis, uveitis, keratitis, esophagitis

SIGNS & SYMPTOMS

- Herpes labialis
 - Painful ulcers around mouth; high fever; sore throat; pharyngeal oedema; myalgia, cervical lymphadenopathy
 - **Recurrent infection:** pain, burning, tingling, vesicle formation
- Genital herpes
 - **Genital ulceration, vesicles:** vulva, cervix, vagina, penis shaft/glans, perineum, buttocks
 - Genital pain, dysuria, fever, neuralgia
 - Constipation, rectal pain, tenesmus, proctitis



Figure 79.3 Blisters on the lips caused by infection with herpes simplex virus.

DIAGNOSIS

LAB RESULTS

- Viral culture
- HSV polymerase chain reaction (PCR)
- Direct fluorescent antibody (DFA) test
- Serological HSV-1/HSV-2 specific IgG assay



Figure 79.4 Blisters on the dorsum of the penis of an individual infected with genital herpes simplex.

TREATMENT

MEDICATIONS

Herpes labialis

- Antivirals (e.g. oral aciclovir, valaciclovir, famciclovir)
- Topical antivirals

Genital herpes

- Antivirals (e.g. oral aciclovir, valaciclovir, famciclovir)
- **Pregnant:** antiviral prophylaxis

OTHER INTERVENTIONS

Genital herpes

- **Pregnant:** possible cesarean delivery

HUMAN HERPESVIRUS 6 (ROSEOLA)

osms.it/human-herpesvirus-6

PATHOLOGY & CAUSES

- Causes roseola (infantum)
- Common cause of fever, followed by rash in early childhood, associated with febrile seizures
- Incubation period
 - 1–2 weeks

CAUSES

- Asymptomatic contacts
 - Person-to-person spread by respiratory secretions
- Tropic for CD4⁺ T lymphocytes

- Following acute infection, remains latent in various tissues

RISK FACTORS

- More common in young children (six months–two years)
- Immunosuppressed
 - Bone marrow/organ transplant
 - Reactivation of latent virus

COMPLICATIONS

- Afebrile **seizures**
- Associated with chronic fatigue syndrome, multiple sclerosis, systemic lupus erythematosus

SIGNS & SYMPTOMS

- 3–5 days of **high fever**; peak in early evening
- **Exanthem**; morbilliform **rash** appears with defervescence; 3–5mm pink/red macules, papules along trunk, extremities
- Diarrhea, tympanic membrane inflammation, upper respiratory symptoms
- **Nagayama's spots**: enanthem of red papules on soft palate, uvula
- Rare
 - Seizures, periorbital oedema, bulging anterior fontanelle, cervical/occipital/postauricular lymphadenopathy

DIAGNOSIS

LAB RESULTS

- Complete blood count
 - ↓ white blood cells
- Detection of HHV-6B/HHV-7
 - Viral culture, specific IgG detection

TREATMENT

- Usually self-limiting

MEDICATIONS

- Immunocompromised
 - Antiviral compounds (e.g. acyclovir, ganciclovir, cidofovir, foscarnet)
- Oral hydration, antipyretics (e.g. paracetamol, ibuprofen)
- Avoid aspirin; may lead to Reye's syndrome



Figure 79.5 A child with roseola infantum, also known as sixth disease. The most common causative agent is human herpes virus six.

HUMAN HERPESVIRUS 8 (KAPOSI'S SARCOMA)

osms.it/human-herpesvirus-8

PATHOLOGY & CAUSES

- Causes Kaposi's sarcoma
 - Low-grade vasoformative neoplasm associated with human herpesvirus-8 (HHV-8) infection/Kaposi's sarcoma herpesvirus (KSHV) infection
- Lesions on mucocutaneous areas; may involve lymph nodes, viscera
- Skin lesions
 - Patch → plaque → ulcerating tumor nodules
- Morphology
 - spindle-shape, vasoformative cells with vascular proliferation, inflammatory cells

- Spontaneous regression may occur after HAART/immunosuppressive treatment

TYPES

- Epidemic AIDS-associated Kaposi's sarcoma
 - HIV-positive individuals
- Classic sporadic Kaposi's sarcoma
 - More common in individuals who are male, older, with Mediterranean/Jewish background
- Iatrogenic, transplant-associated Kaposi's sarcoma
 - Solid organ transplant individuals
- African endemic Kaposi's sarcoma
 - More common in central Africa, unrelated to HIV

RISK FACTORS

- More common in individuals who are biologically male, > 50 years
- Immunosuppression, HIV (co-infection synergistic → aggressive, widespread); drug abuse; immunosuppression therapy

COMPLICATIONS

- Secondary skin lesion infection

SIGNS & SYMPTOMS

- Skin lesions
 - Multifocal; asymmetrically distributed; size, colour variation; non-pruritic; papular; nodular; plaque-, bullous-like; indurated; hyperkeratotic
- Oral lesions
 - Hard palate, gingiva, dorsum of tongue
 - Macules, papules, nodules, exophytic masses
- Lymphadenopathy, lymphoedema
- Fever, weight loss, night sweats

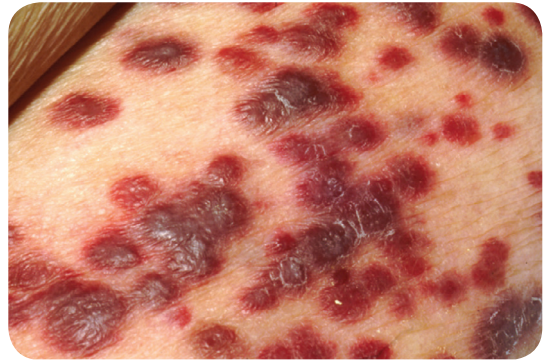


Figure 79.6 The skin of an individual with Kaposi's sarcoma.

DIAGNOSIS

DIAGNOSTIC IMAGING

Chest X-ray

- Nodular/interstitial/alveolar infiltrates; hilar/mediastinal lymphadenopathy; nodules

LAB RESULTS

- HIV test
- Positive in AIDS-associated Kaposi's sarcoma
- Fecal occult blood
 - Positive may indicate intestinal lesions

OTHER DIAGNOSTICS

- Lesion, lymph node biopsy of vascular lesion

TREATMENT

MEDICATIONS

- Delay disease progression
 - HAART; in HIV infected individuals, HIV suppression may shrink Kaposi's sarcoma lesions; systemic chemotherapy
- Cosmetic
 - Topical retinoids; intralesional vinblastine

SURGERY

- Cosmetic
 - Surgical excision; cryotherapy; laser therapy (external beam radiation)

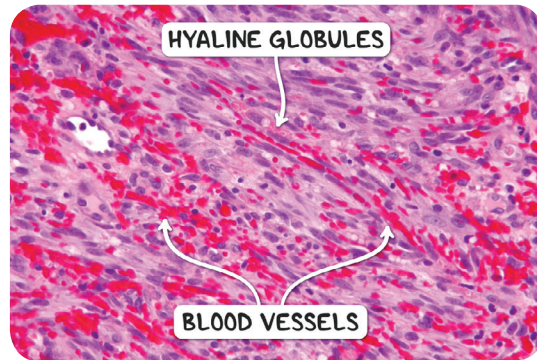


Figure 79.7 The histological appearance of a Kaposi sarcoma. The tumor is composed of spindle cells and numerous branching vascular spaces. The occasional spindle cell contains hyaline globules.

VARICELLA ZOSTER VIRUS

osms.it/varicella-zoster-virus

PATHOLOGY & CAUSES

- Double-stranded, linear DNA virus
 - Causes chickenpox, shingles
 - **Chickenpox**: generally benign, self-limited disease in immunocompetent children
 - **Shingles**: painful skin rash, can occur in individuals who have recovered from primary VZV infection

Primary infection (chickenpox)

- **Transmission**: airborne spread through aerosolized droplets, direct lesion contact
- VZV enters respiratory system → lymph node spread → targets skin, mucous membranes → small blood vessel vasculitis → epithelial cell degeneration → fluid-filled vesicles
 - **Incubation period**: 14 days
 - **Most infectious**: 1–2 days before rash; infectious 3–4 days, until lesions crusted
 - After symptoms resolve, VZV dormant in nervous system; latent in trigeminal, dorsal root ganglia



Figure 79.8 A child with chickenpox.

Secondary infection (shingles)

- Occurs when **dormant VZV reactivates**
 - Reactivation in dorsal root, cranial nerve ganglia → travels down axons → local skin inflammation innervated by ganglion
 - Prodromal 2–4 day tingling/localized pain before rash onset

RISK FACTORS

Chickenpox

- More common in children
 - 1–9 years old (highest risk)
- Non-immunized status
- Immunocompromised status

Shingles

- Primary varicella infection history
- More common in adults
 - > 50 years old (highest risk)
- **Immunocompromised** status
- Stress

COMPLICATIONS

Chickenpox

- Secondary bacterial infection, cutaneous scarring, encephalopathy, varicella pneumonitis/pneumonia
- Central nervous system (CNS) complications
 - Meningitis, encephalitis, intracranial vasculitis
- Congenital varicella syndrome
 - Limb hypoplasia, paresis, microcephaly, ophthalmic lesions

Shingles

- Ramsay Hunt syndrome
 - VZV of geniculate ganglion affects facial nerve; hearing loss, facial weakness
- **Postherpetic neuralgia**, superinfection of skin lesions, encephalitis, Mollaret's meningitis, zoster multiplex/sine herpete, stroke, myelitis
- **Herpes zoster ophthalmicus** (sight-threatening)

SIGNS & SYMPTOMS

Chickenpox

- Fever, headache, malaise, sore throat, tachycardia
- Rash characteristics
 - Generalized pruritic, **vesicular rash**
 - “Dew drop on rose petal” appearance
 - **Formation:** macules → **vesicles** → rupture → scab
 - Vesicles on mucous membranes (e.g. nasopharynx, conjunctiva, mouth, vulva)

Shingles

- Erythematous, maculopapular lesions evolve into painful **vesicular rash**
 - Rash **follows dermatomal distribution** of cranial nerve/dorsal root ganglion
 - Thoracic, lumbar dermatomes most commonly affected



Figure 79.9 Herpes zoster, or shingles, affecting the ophthalmic branch of the trigeminal nerve.



Figure 79.10 Herpes zoster in a dermatomal distribution on the chest.

DIAGNOSIS

LAB RESULTS

- Microbe identification
 - PCR: VZV DNA
 - Viral culture: positive VZV
 - DFA: VZV antigen

TREATMENT

MEDICATIONS

Chickenpox

- *Low risk*: usually self-limiting
- *Moderate risk*: oral antiviral therapy
- *High risk*: intravenous antiviral therapy; zoster-immune globulin (ZIG)

Shingles

- Oral/intravenous antiviral therapy
- Analgesics
 - E.g. paracetamol, ibuprofen; topical; opioid
- Calamine lotion
- Varicella-zoster immune globulin

OTHER INTERVENTIONS

- Prevention
 - Live attenuated VZV vaccine